

IT IS CLAIMED:

1. An isolated nucleic acid molecule that encodes an ovine interferon- $\gamma$ .

2. A nucleic acid of claim 1, where said nucleic acid molecule has the sequence presented as SEQ ID NO:1.

3. A nucleic acid molecule of claim 1, wherein said nucleic acid molecule encodes a polypeptide having a sequence presented as SEQ ID NO:2.

4. A nucleic acid of claim 3, where said polypeptide includes a leader sequence.

5. An expression vector comprising  
(a) a nucleic acid containing an open reading frame that encodes the ovine interferon- $\gamma$ ; and  
(b) regulatory sequences effective to express said open reading frame in a host cell.

6. A method of recombinantly producing ovine interferon- $\gamma$ , comprising  
introducing into suitable host cells, a recombinant expression system containing an open reading frame (ORF) having a polynucleotide sequence which encodes an ovine interferon- $\gamma$  polypeptide, where the vector is designed to express the ORF in said host, and  
culturing said host under conditions resulting in the expression of the ORF sequence.

7. A recombinantly produced ovine interferon- $\gamma$  protein.

8. The recombinantly produced protein of claim 7, where said protein has the sequence presented as SEQ ID NO:2.

5 9. A method of inhibiting tumor cell growth, comprising

contacting the cells with ovine interferon- $\gamma$  at a concentration effective to inhibit growth of the tumor cells.

10 10. A method of inhibiting viral replication, comprising

15 contacting cells infected with a virus with ovine interferon- $\gamma$  at a concentration effective to inhibit viral replication within said cells.

11. The method of claim 10, where said virus is an RNA virus.

20 12. The method of claim 11, where said virus is selected from the group consisting of feline leukemia virus, ovine lentivirus, equine infectious anemia virus, bovine immunodeficiency virus, visna-maedi virus, and caprine arthritis encephalitis.

25 13. The method of claim 10, where said virus is a DNA virus.

30 14. The method of claim 10, where said interferon- $\gamma$  has the protein sequence presented as SEQ ID NO:2.

35 15. An isolated nucleic acid molecule that encodes a human interferon- $\gamma$ .

16. A nucleic acid of claim 15, where said nucleic acid molecule includes the sequence presented as SEQ ID NO:43.

5 17. A nucleic acid molecule of claim 15, wherein said nucleic acid molecule encodes a polypeptide having a sequence presented as SEQ ID NO:44.

10 18. A nucleic acid molecule of claim 17, where said polypeptide further includes a leader sequence.

15 19. A nucleic acid of claim 15, where said nucleic acid molecule includes the sequence presented as SEQ ID NO:29.

20 20. A nucleic acid molecule of claim 15, wherein said nucleic acid molecule encodes a polypeptide having a sequence presented as SEQ ID NO:30.

25 21. A nucleic acid molecule of claim 20, where said polypeptide further includes a leader sequence.

30 22. A nucleic acid of claim 15, where said nucleic acid molecule includes the sequence presented as SEQ ID NO:33.

23. A nucleic acid molecule of claim 15, wherein said nucleic acid molecule encodes a polypeptide having a sequence presented as SEQ ID NO:34.

24. A nucleic acid molecule of claim 23, where said polypeptide further includes a leader sequence.

25. A nucleic acid of claim 15, where said nucleic acid molecule includes the sequence presented as SEQ ID NO:25.

5           26. A nucleic acid molecule of claim 15, wherein said nucleic acid molecule encodes a polypeptide having a sequence presented as SEQ ID NO:26.

10           27. A nucleic acid molecule of claim 26, where said polypeptide further includes a leader sequence.

15           28. A nucleic acid of claim 15, where said nucleic acid molecule includes the sequence presented as SEQ ID NO:27.

20           29. A nucleic acid molecule of claim 15, wherein said nucleic acid molecule encodes a polypeptide having a sequence presented as SEQ ID NO:28.

25           30. A nucleic acid molecule of claim 29, where said polypeptide further includes a leader sequence.

30           31. A nucleic acid of claim 15, where said nucleic acid molecule includes the sequence presented as SEQ ID NO:21.

35           32. A nucleic acid molecule of claim 15, wherein said nucleic acid molecule encodes a polypeptide having a sequence presented as SEQ ID NO:22.

40           33. A nucleic acid molecule of claim 32, where said polypeptide further includes a leader sequence.

34. A nucleic acid of claim 15, where said nucleic acid molecule includes the sequence presented as SEQ ID NO:23.

5           35. A nucleic acid molecule of claim 15, wherein said nucleic acid molecule encodes a polypeptide having a sequence presented as SEQ ID NO:24.

10           36. A nucleic acid molecule of claim 35, where said polypeptide further includes a leader sequence.

          37.- An expression vector comprising  
          (a) a nucleic acid containing an open  
reading frame that encodes a human interferon- $\gamma$ ; and  
15           (b) regulatory sequences effective to  
express said open reading frame in a host cell.

          38. An expression vector of claim 37, where said human interferon- $\gamma$  contains a polypeptide having a  
20           sequence presented as SEQ ID NO:44.

          39. An expression vector of claim 37, where said human interferon- $\gamma$  contains a polypeptide having a  
sequence presented as SEQ ID NO:30.

25           40. An expression vector of claim 37, where said human interferon- $\gamma$  contains a polypeptide having a  
sequence presented as SEQ ID NO:34.

30           41. An expression vector of claim 37, where said human interferon- $\gamma$  contains a polypeptide having a  
sequence presented as SEQ ID NO:26.

42. An expression vector of claim 37, where said human interferon- $\gamma$  contains a polypeptide having a sequence presented as SEQ ID NO:28.

5 43. An expression vector of claim 37, where said human interferon- $\gamma$  contains a polypeptide having a sequence presented as SEQ ID NO:22.

10 44. An expression vector of claim 37, where said human interferon- $\gamma$  contains a polypeptide having a sequence presented as SEQ ID NO:24.

45. A method of recombinantly producing human interferon- $\gamma$ , comprising  
15 introducing into suitable host cells, a recombinant expression system containing an open reading frame (ORF) having a polynucleotide sequence which encodes a human interferon- $\gamma$  polypeptide, where the vector is designed to express the ORF in said host,  
20 and  
culturing said host under conditions resulting in the expression of the ORF sequence.

25 46. An isolated human interferon- $\gamma$  protein.

47. A protein of claim 46, where said protein is recombinantly produced.

30 48. A protein of claim 46, where said protein contains the sequence presented as SEQ ID NO:44.

49. A protein of claim 46, where said protein contains the sequence presented as SEQ ID NO:30.

50. A protein of claim 46, where said protein contains the sequence presented as SEQ ID NO:34.

51. A protein of claim 46, where said protein contains the sequence presented as SEQ ID NO:26.

52. A protein of claim 46, where said protein contains the sequence presented as SEQ ID NO:28.

53. A protein of claim 46, where said protein contains the sequence presented as SEQ ID NO:22.

54. A protein of claim 46, where said protein contains the sequence presented as SEQ ID NO:24.

55. A method of inhibiting tumor cell growth, comprising  
contacting the cells with human interferon- $\gamma$  at a concentration effective to inhibit growth of the tumor cells.

56. A method of claim 55, wherein said cells are human carcinoma cells, human leukemia cells, human T-lymphoma cells, and human melanoma cells.

57. A method of claim 56, wherein said cells are steroid-sensitive tumor cells.

58. A method of claim 57, wherein said cells are mammary tumor cells.

59. A method of claim 55, where said protein contains the sequence presented as SEQ ID NO:44.

60. A method of claim 55, where said protein contains the sequence presented as SEQ ID NO:30.

5 61. A method of claim 55, where said protein contains the sequence presented as SEQ ID NO:34.

62. A method of claim 55, where said protein contains the sequence presented as SEQ ID NO:26.

10 63. A method of claim 55, where said protein contains the sequence presented as SEQ ID NO:28.

15 64. A method of claim 55, where said protein contains the sequence presented as SEQ ID NO:22.

65. A method of claim 55, where said protein contains the sequence presented as SEQ ID NO:24.

20 66. A method of inhibiting viral replication, comprising  
contacting cells infected with a virus with human interferon- $\gamma$  at a concentration effective to inhibit viral replication within said cells.

25 67. A method of claim 66, where said virus is an RNA virus.

30 68. A method of claim 67, where said virus is human immunodeficiency virus, or hepatitis c virus.

69. A method of claim 66, where said virus is a DNA virus.

35 70. A method of claim 69, where said virus is hepatitis B virus.



71. A method of claim 66, where said protein contains the sequence presented as SEQ ID NO:44.

5 72. A method of claim 66, where said protein contains the sequence presented as SEQ ID NO:30.

73. A method of claim 66, where said protein contains the sequence presented as SEQ ID NO:34.

10 74. A method of claim 66, where said protein contains the sequence presented as SEQ ID NO:26.

15 75. A method of claim 66, where said protein contains the sequence presented as SEQ ID NO:28.

76. A method of claim 66, where said protein contains the sequence presented as SEQ ID NO:22.

20 77. A method of claim 66, where said protein contains the sequence presented as SEQ ID NO:24.

25 78. A method of enhancing fertility in a female mammal, comprising  
administering to said mammal an effective  
mammalian fertility enhancing amount of human  
interferon- $\gamma$  in a pharmaceutically acceptable carrier.

30 79. A method of claim 78, where said protein contains the sequence presented as SEQ ID NO:44.

80. A method of claim 78, where said protein contains the sequence presented as SEQ ID NO:30.

35 81. A method of claim 78, where said protein contains the sequence presented as SEQ ID NO:34.

82. A method of claim 78, where said protein contains the sequence presented as SEQ ID NO:26.

5 83. A method of claim 78, where said protein contains the sequence presented as SEQ ID NO:28.

84. A method of claim 78, where said protein contains the sequence presented as SEQ ID NO:22.

10 85. A method of claim 78, where said protein contains the sequence presented as SEQ ID NO:24.

86. A fused polypeptide, comprising:

15 (a) an interferon- $\gamma$  polypeptide, where said polypeptide is (i) derived from an interferon- $\gamma$  amino acid coding sequence, and (ii) between 15 and 172 amino acids long; and

(b) a second soluble polypeptide.

20 87. The fused polypeptide of claim 86, wherein said interferon- $\gamma$  polypeptide is selected from the group consisting of SEQ ID NO:5 and SEQ ID NO:15.

25 88. The fused polypeptide of claim 86, wherein said second soluble polypeptide is interferon- $\alpha$ .

89. The fused polypeptide of claim 86, wherein said second soluble polypeptide is interferon- $\beta$ .

30 90. An interferon- $\gamma$ /type I interferon fusion protein comprising:

a type I interferon protein wherein the N-terminal cytotoxic region of said type I interferon is replaced by an N-terminal region of interferon- $\gamma$  within a  
35 sequence spanning residues 1 to 37 of interferon- $\gamma$ ,

and the fusion protein has reduced cytotoxicity  
relative to the cytotoxicity of the type I interferon.

5 91. The fusion protein of claim 90, wherein said  
type I interferon is interferon- $\alpha$ .

92. The fusion protein of claim 90, wherein said  
type I interferon is interferon- $\beta$ .

10 93. The fusion protein of claim 90, wherein said  
interferon- $\gamma$  is ovine, bovine, or human interferon- $\gamma$ .

15 94. The fusion protein of claim 90, wherein the  
sequence from residues 1 to 37 is SEQ ID NO:5 and the  
sequence from residues 38 to the C-terminal residue is  
the corresponding sequence of said type I interferon.

20 95. The fusion protein of claim 90, wherein the  
sequence from residues 1 to 37 is SEQ ID NO:15 and the  
sequence from residues 38 to the C-terminal residue is  
the corresponding sequence of said type I interferon.